Dolly et al., Modification of Clostridial Toxins for Use as Transport Proteins

## **AMENDMENTS**

## Amendments to the Claims

- 1-30. (Canceled)
- 31. (Currently amended) A composition comprising a Clostridial neurotoxin joined to a drug.
  - i) a Clostridial neurotoxin light chain which has enzymatic activity for a target substrate selected from the group consisting of SNAP-25, VAMP and Cellubrevin, and
  - ii) a Clostridial neurotoxin heavy chain which has binding specificity for a target nerve cell; and
  - b) a drug or other bioactive molecule joined to the light chain of the active neurotoxin,
    wherein the active neurotoxin is internalizable by the target nerve cell.
- 32. (Currently amended) The composition of claim 31 wherein said Clostridial neurotoxin is an active Clostridial neurotoxin. the neurotoxin comprises a light chain selected from the group consisting of: tetanus toxin, botulinum toxin A, botulinum toxin B, botulinum toxin C, botulinum toxin D, botulinum toxin E, botulinum toxin F, and botulinum toxin G.
- 33. (Cancelled)
- 34. (Currently amended) The composition of claim 31 wherein said drug is an intracellular acting drug. the neurotoxin comprises a heavy chain selected from the group consisting of: tetanus toxin, botulinum toxin A, botulinum toxin B, botulinum toxin C, botulinum toxin D, botulinum toxin E, botulinum toxin F, and botulinum toxin G.
- 35-36 (Cancelled)
- 37. (New) A pharmaceutical composition for treatment of a neuromuscular dysfunction in a mammal, comprising:
  - a) a Clostridial neurotoxin comprising
    - a Clostridial neurotoxin light chain which has enzymatic activity for a target substrate selected from the group consisting of SNAP-25, VAMP and Cellubrevin, and
    - ii) a Clostridial neurotoxin heavy chain which has binding specificity for a target nerve cell; and
  - b) a drug or other bioactive molecule joined to the light chain of the active neurotoxin,
  - wherein the active neurotoxin is internalizable by the target nerve cell and a pharmaceutically acceptable excipient.

38. (New) The pharmaceutical composition of claim 37 wherein the neurotoxin comprises a light chain selected from the group consisting of: tetanus toxin, botulinum toxin A, botulinum toxin B, botulinum toxin C, botulinum toxin D, botulinum toxin E, botulinum toxin F, and botulinum toxin G.

- 39. (New) The pharmaceutical composition of claim 37 wherein the neurotoxin comprises a heavy chain selected from the group consisting of: tetanus toxin, botulinum toxin A, botulinum toxin B, botulinum toxin C, botulinum toxin D, botulinum toxin E, botulinum toxin F, and botulinum toxin G.
- 40. (New) The pharmaceutical composition of claim 37 wherein the neuromuscular dysfunction is characterized by uncontrollable muscle spasms.
- 41. (New) The composition of either of claims 31 or 37 wherein the drug or other bioactive molecule is an inhibitor of neurotransmitter release.
- 42. (New) The composition of either of claims 31 or 37 wherein the drug or other bioactive molecule is an active ingredient for treatment of botulism or tetanus.
- 43. (New) The composition of either of claims 31 or 37 wherein the drug or other bioactive molecule is selected from the group consisting of a GABA agonist, a neuronal calcium channel agonist, an adenosine agonist, a glutamate antagonist, a protein synthesis toxin, a zinc-dependent protease inhibitor, a neuronal growth factor, an antiviral agent, a nicotinic antagonist, a neuronal calcium channel blocker, an acetylcholine esterase inhibitor, a potassium channel activator, a vasamicol or a vasamicol inhibitor, a ribozyme, and a transcribable gene.